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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/200,657	11/25/1998	MICH B. HEIN	TSRI-184.2CO	9640

7590 01/02/2003
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EXAMINER

COLLINS, CYNTHIA E

ART UNIT PAPER NUMBER

1638

DATE MAILED: 01/02/2003

39

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/200,657

Applicant(s)

HEIN ET AL.

Examiner

Cynthia Collins

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43,44,48,53,57-59,79,81-90 and 93-99 is/are pending in the application.
- 4a) Of the above claim(s) 43,44,48,53,57-59 and 96-99 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 79,81-90 and 93-95 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 4, 2002 has been entered.

The Amendments filed March 4, 2002 and May 30, 2002 have been entered.

The Declaration filed March 15, 2002 has been entered.

The supplemental responses filed March 15, 2002 and May 3, 2002 have been entered.

Claims 21, 32-42, 45-47, 49-52, 54, 56, 60-66, 68-78, 80 and 91-92 have been cancelled.

Claims 43, 79, 81, 82 and 83 have been amended.

Claims 83-89 have been added.

Claims 43-44, 48, 53, 57-59, 79, 81-90 and 93-99 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Election/Restrictions

Applicant's election with traverse of Group II, claims 79, 81-90 and 93-95, drawn to a plant comprising cells containing nucleotide sequence encoding an immunoglobulin single polypeptide product containing at least an immunoglobulin heavy chain polypeptide, in Paper

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No. 38 is acknowledged. The traversal is on the ground(s) that a search and examination of both groups would not be unduly burdensome as both groups are directed to immunoglobulin polypeptides expressed in plants, and because the application claims priority to prior cases directed to the same art. This is not found persuasive because the Groups are directed to different types of immunoglobulin polypeptides expressed in plants, and while the searches of both groups may overlap with each other as well as with the prior cases to which the instant application claims priority, their searches are not coextensive. Accordingly, claims 43-44, 48, 53, 57-59 and 96-99 are withdrawn from consideration as being directed to nonelected inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claim 79 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 79 is dependent on claim 43, which is not a previous claim.

Claim 79 is objected to for being dependent on a claim directed to a nonelected invention (claim 43). Appropriate correction is required.

Double Patenting

Claims 79, 81-90 and 93-95 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21-66 of

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copending Application No. 09/512736, for the reasons of record set forth in the office action mailed July 5, 2001.

The Office acknowledges Applicant's request that the terminal disclaimer filed with the previous amendment be entered in the case in order to overcome the rejection (reply March 4, 2002, page 9).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 83-90 and 93-95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 83, and claims 84-90 and 93-95 dependent thereon, is indefinite in the recitation of "said nucleotide sequences" in part b). There is insufficient antecedent basis in claim 83 for the limitation "said nucleotide sequences", as part a) of claim 83 recites "nucleotide sequence" in the singular.

Claim 83, and claims 84-90 and 93-95 dependent thereon, is indefinite in the recitation of "derived". It is unclear what part of the heavy chain is derived from an antigen-specific immunoglobulin and what part of the heavy chain is retained by an antigen-specific immunoglobulin. It is suggested that the claim be amended to recite "obtained" rather than "derived".

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Claim 84, and claims 85-87 dependent thereon, is indefinite in the recitation of "is a multimer". It is unclear how a single polypeptide product also could be a multimer, as a multimer by definition is comprised of multiple polypeptides.

Claim Rejections - 35 USC § 102

Claims 81-83, 88-90 and 93 are rejected under 35 U.S.C. 102(b) as being anticipated by During (Dissertation, July 9, 1988, University of Koln, FRG, English translation), for the reasons of record set forth in the office action mailed July 5, 2001.

Applicant's arguments filed March 4, 2002, April 29, 2002, May 30, 2002 and September 6, 2002, have been fully considered but they are not persuasive.

Applicant argues that During fails to disclose a plant comprising cells containing a nucleic acid encoding an immunoglobulin single polypeptide product, that During fails to disclose plant cells containing an assembled antigen-specific single polypeptide product following proteolytic processing of a leader sequence, that During made no attempt to express a heavy chain polypeptide without a light chain polypeptide, that During does not disclose the requirement for a single polynucleotide encoding a single polypeptide product, that During does not disclose the requirement for a plant cell comprising a heavy chain alone or a light chain alone such that each chain could assemble into an antigen specific immunoglobulin if expressed with the other chain, and that During never demonstrated the production of a heavy chain. Applicant also argues that there was a prejudice in the art against the possibility that plant cells could be used to produce an antigen specific immunoglobulin, and a prejudice in the art against the possibility of using plant cells to process and assemble an antigen specific immunoglobulin, due

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to the complexity of the native process as it occurs in B cells. Applicant also argues that During's experimental results are internally consistent and lack critical controls (reply March 4, 2002 pages 9-10; reply April 29, 2002 pages 2-10; reply May 30, 2002 pages 6-7; reply September 6, 2002 page 7).

The Office maintains that the plants as currently claimed are not limited to plants whose cells containing only a nucleic acid encoding an immunoglobulin single polypeptide product. The claims are drawn to a plant comprising plant cells containing a nucleotide sequence encoding an immunoglobulin single polypeptide product containing an immunoglobulin heavy chain polypeptide, and the immunoglobulin single polypeptide product encoded by said sequence. The claimed plants are not limited to plants whose cells contain only a nucleic acid encoding an immunoglobulin single polypeptide product as "containing" is inclusive or open-ended and does not exclude additional, unrecited elements. Accordingly, the plants taught by During et al. contain a nucleotide sequence encoding an immunoglobulin single polypeptide product containing an immunoglobulin heavy chain polypeptide containing an immunoglobulin heavy chain polypeptide, even though the plants taught by During et al. also contain a nucleotide sequence encoding an immunoglobulin light chain polypeptide as well. Furthermore, the plants taught by During et al. necessarily contain the immunoglobulin single polypeptide heavy chain product encoded by said heavy chain encoding sequence, as B1-8 antibody was detected in the plants taught by During (page 112). Additionally, the claims do not require a plant cell comprising a heavy chain alone or a light chain alone such that each chain could assemble into an antigen specific immunoglobulin if expressed with the other chain. The claims require that the single polypeptide heavy chain product be capable of forming an antigen-specific

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immunoglobulin when co-expressed in the same cell with a light chain polypeptide. The capacity to form an antigen-specific immunoglobulin with a light chain polypeptide merely describes an inherent property of the heavy chain polypeptide.

Finally, regarding the assertion of prejudice in the art against the possibility of using plant cells to process and assemble an antigen specific immunoglobulin, the Office notes that the rejected claims are not directed to a processed and assembled antigen specific immunoglobulin. Regarding the assertion that During's experimental results are internally consistent and lack critical controls, the Office notes that Applicant's arguments and the Lerner declaration are primarily directed to the production of fully assembled antibody molecules in plants, and thus are not commensurate in scope with the claimed invention, which is not limited to fully assembled antibody molecules.

Claims 81-83, 88-90 and 93-94 are rejected under 35 U.S.C. 102(e) as being anticipated by Goodman (US Patent No. 4956282), for the reasons of record set forth in the office action mailed July 5, 2001.

Applicant's arguments filed March 4, 2002, April 29, 2002, May 30, 2002 and September 6, 2002, have been fully considered but they are not persuasive.

Applicant argues that Goodman's passing reference entirely misses the idea of preparing plant cells containing a nucleotide sequence encoding an immunoglobulin single polypeptide product, and that Goodman never attempted to express an immunoglobulin in a plant (reply March 4, 2002 pages 11-12; reply April 29, 2002 page 11; reply May 30, 2002 page 7; reply September 6, 2002 page 7).

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As discussed *supra*, the Office maintains that the plants as currently claimed are not limited to plants whose cells containing only a nucleic acid encoding an immunoglobulin single polypeptide product. The Office also maintains that while Goodman did not express an immunoglobulin in a plant, Goodman is enabled for the expression of any heterologous single chain polypeptide product in plant cells absent evidence to the contrary.

Claim Rejections - 35 USC § 103

Claims 79, 81-90 and 93-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over During (Dissertation, July 9, 1988, University of Koln, FRG, English translation) in view of Applicant's admitted prior art for the reasons of record set forth in the office action mailed July 5, 2001.

Applicant's arguments filed March 4, 2002, April 29, 2002, May 30, 2002 and September 6, 2002, have been fully considered but they are not persuasive.

Applicant argues that During does not teach a plant comprising cells containing a nucleic acid encoding any immunoglobulin single polypeptide product, and During teaches away from the claimed invention as During failed to detect expression of light chain alone and never attempted expression of heavy chain alone Applicant also argues that the prior art of Goodman does not remedy the deficiencies of During as Goodman only teaches expression of immunoglobulin heavy and light chains together (reply March 4, 2002 pages 14-15; reply April 29, 2002 pages 14-15; reply May 30, 2002 page 7; reply September 6, 2002 page 7).

As discussed *supra*, the Office maintains that the plants as currently claimed are not limited to plants whose cells containing only a nucleic acid encoding an immunoglobulin single

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polypeptide product. Furthermore, the teachings of Goodman are not limited to the expression of immunoglobulin heavy and light chains together, as Goodman refers to the structural genes of both the light chain and the heavy chain, with the proviso that assembly of the light and heavy chains within the plant cells would be desirable (column 3 lines 21-23).

Claims 79, 81-90 and 93-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman (US Patent No. 4956282) in view of Applicant's admitted prior art for the reasons of record set forth in the office action mailed July 5, 2001.

Applicant's arguments filed March 4, 2002, April 29, 2002, May 30, 2002 and September 6, 2002, have been fully considered but they are not persuasive.

Applicant argues that Goodman fails to mention, teach or suggest a plant comprising plant cells containing a nucleic acid encoding a single polypeptide product comprising a heavy chain alone, or a heavy chain, that Goodman does not enable expression of a dual chain immunoglobulin, or the expression of a heavy chain polypeptide in a manner that allows it to form an antigen-specific immunoglobulin when coexpressed with the light chain, that the gamma interferon polypeptide expressed by Goodman is naturally expressed as a single polypeptide whereas heavy chain and light chain polypeptides are naturally co-expressed. Applicant argues that Goodman's teachings would not reasonably have been considered to advance the possibility of expressing a single heavy chain polypeptide separately in plants, as gamma interferon is structurally and functionally distinct from immunoglobulins. Applicant also points out that expression of heavy chain in the absence of light chain is toxic to B cells, and that During's failure to detect light chain expression would negate any teaching on the part of Goodman (reply

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March 4, 2002 pages 16-17; reply April 29, 2002 pages 17-18; reply May 30, 2002 pages 8-9; reply September 6, 2002 page 9).

As discussed *supra*, the Office maintains that the plants as currently claimed are not limited to plants whose cells containing only a nucleic acid encoding an immunoglobulin single polypeptide product. As discussed *supra*, the claims also do not require the expression of a heavy chain polypeptide in a manner that allows it to form a antigen-specific immunoglobulin when coexpressed with the light chain. The Office further maintains that Goodman's expression of a heterologous interferon polypeptide in plant cells would reasonably have been considered to advance the possibility of expressing any single chain heterologous polypeptide in a plant cell. While gamma interferon is structurally and functionally distinct from immunoglobulins, both gamma interferon and immunoglobulins are heterologous to plants. With respect to the toxicity of heavy chain expression in the absence of light chain expression in B cells, the prior art teaches that the toxicity of heavy chain expression in the absence of light chain expression is not a universal phenomenon for all cell types. See for example Dorai et al. who observed no cellular toxicity of unassembled heavy chain monomer expressed in myeloma cells (The Journal of Immunology, December 15, 1987, Vol. 139, No. 12, pages 4232-4241). Furthermore, During's failure to detect light chain expression would not negate the teachings of Goodman, as the plants taught by During et al. necessarily contain both heavy and light chain immunoglobulin products, as B1-8 antibody was detected in the plants taught by During (page 112).

Remarks

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210.

The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
December 23, 2002

Phuong T. Bui 12/26/02

PHUONG T. BUI
PRIMARY EXAMINER